# **AMENDMENTS TO THE CLAIMS**

Docket No.: 61387(72021)

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently amended) A compound of the formula:

or a pharmaceutically acceptable salt thereof, wherein:

n is 0 or 1;

W, X and Y are each independently N or CR<sub>1</sub>;

 $A_1$ ,  $A_2$ ,  $A_3$  and  $A_4$  are each independently N or  $CR_4$ ;

B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, B<sub>4</sub> and B<sub>5</sub> are each independently N or CR<sub>5</sub>;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, nitro, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>aminosulfonyl, C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- or di- $(C_1-C_6alkyl)aminoC_0-C_4alkyl;$ 

 $R_2$  is cyano, cyano $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkylsulfonyl, halo $C_1$ - $C_6$ alkyl)aminosulfonyl or mono- or di- $(C_1$ - $C_6$ alkyl)aminocarbonyl;

R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:  $R_x$  is  $C_0$ - $C_3$ alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

Docket No.: 61387(72021)

M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $\underline{C_8}$ alkenyl- $\underline{C_1}$ - $\underline{C_8}$ alkenyl-or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl $\underline{C_1}$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

# R<sub>v</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with  $R_x$  or  $R_z$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

### R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>4</sub> is independently selected at each occurrence from R<sub>b</sub>, or two adjacent R<sub>4</sub> groups are taken together to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>;

Docket No.: 61387(72021)

R<sub>5</sub> is independently selected at each occurrence from R<sub>b</sub>, or two adjacent R<sub>5</sub> groups are taken together to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_3$ - $C_8$ cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di- $(C_1-C_4alkyl)$ amino.
  - 2. (Original) A compound or salt according to claim 1, wherein Y is N.
- 3. (Currently amended) A compound or salt according to claim 1-or claim 2, wherein W is N and X is CR<sub>1</sub>.
- 4. (Currently amended) A compound or salt according to claim 1-or claim 2, wherein X is N and W is CR<sub>1</sub>.
- 5. (Currently amended) A compound or salt according to any one of claims 1-4claim 1, wherein n is 0.
- (Currently amended) A compound or salt according to any one of 6. claims 1-5claim 1, wherein A<sub>2</sub> and A<sub>3</sub> are C-CH<sub>3</sub>, C-halogen or CH.

7. (Original) A compound or salt according to claim 6, wherein  $A_2$  and  $A_3$  are CH.

Docket No.: 61387(72021)

- 8. (Currently amended) A compound or salt according to any one of claims 1-7claim 1, wherein  $A_1$  and  $A_4$  are independently N or CH.
- 9. (Currently amended) A compound or salt according to any one of claims 1-8claim 1, wherein each  $R_4$  is independently chosen from hydrogen, halogen, cyano,  $C_1$ - $C_6$ alkyl,  $\underline{C_2$ - $\underline{C_6}$ alkenyl $\underline{C_4}$ - $\underline{C_6}$ alkenyl, halo $\underline{C_1}$ - $\underline{C_6}$ alkoxy.
- 10. (Currently amended) A compound or salt according to any one of elaims 1-9claim 1, wherein at least two of  $B_1$ ,  $B_2$ ,  $B_3$ ,  $B_4$  and  $B_5$  are  $CR_5$ , and wherein at least one  $R_5$  is not hydrogen.
- 11. (Original) A compound or salt according to claim 10, wherein each  $R_5$  is independently chosen from hydrogen, halogen, cyano, -COOH,  $C_1$ - $C_6$ alkyl,  $\underline{C}_2$ - $\underline{C}_6$ alkenyl $C_1$ - $C_6$ alkenyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy and halo $C_1$ - $C_6$ alkoxy.
- 12. (Currently amended) A compound or salt according to any one of claims 1-11 claim 1, wherein  $R_2$  is trifluoromethyl, methylsulfonyl, trifluoromethylsulfonyl or 2-cyano-prop-2-yl.
- 13. (Currently amended) A compound or salt according to any one of elaims 1-12claim 1, wherein  $R_3$  is:
  - (a) hydrogen, halogen or cyano; or
  - (b) C<sub>1</sub>-C<sub>6</sub>alkyl, <u>C<sub>2</sub>-C<sub>6</sub>alkenyl</u>C<sub>1</sub>-C<sub>6</sub>alkenyl, C<sub>2</sub>-C<sub>6</sub>alkyl ether, mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl or (4- to 10-membered heterocycloalkyl)C<sub>0</sub>-C<sub>6</sub>alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, and haloC<sub>1</sub>-C<sub>4</sub>alkyl.

Page 6

14. (Original) A compound or salt according to claim 13, wherein  $R_3$  is hydrogen.

Docket No.: 61387(72021)

- 15. (Original) A compound or salt according to claim 13, wherein  $R_3$  is  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl or (4- to 10-membered heterocycloalkyl) $C_0$ - $C_6$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, methyl and ethyl.
  - 16. (Currently amended) A compound of the formula:

or a pharmaceutically acceptable salt thereof, wherein:

n is 0 or 1;

- W, X and Y are each independently N or CR<sub>1</sub>;
- $A_1$ ,  $A_2$ ,  $A_3$  and  $A_4$  are each independently N or  $CR_4$ ; such that  $A_2$  and  $A_3$  are not  $C_1$ - $C_6$ alkyl;
- $B_1,\,B_2,\,B_3,\,B_4$  and  $B_5$  are each independently N or  $CR_5;$
- R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, C₁-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkoxy, cvano, nitro, amino, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, aminosulfonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C₁-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di- $(C_1-C_6alkyl)aminoC_0-C_4alkyl;$
- $R_2$  is halogen, cyano, amino,  $C_3$ - $C_6$ alkyl, cyano $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl,  $C_1$ - $C_6$ alkylsulfonyl, halo $C_1$ - $C_6$ alkyl)aminosulfonyl, or mono- or di- $(C_1$ - $C_6$ alkyl)aminocarbonyl;

### R<sub>3</sub> is:

- (i) hydrogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>),  $N(R_z)(C=O)_p$ , SO<sub>2</sub>N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

Docket No.: 61387(72021)

M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $C_8$ alkenyl- $\underline{C_1$ - $C_8$ alkenyl-or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl $\underline{C_1$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

### R<sub>v</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with  $R_x$  or  $R_z$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

#### R<sub>7</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with  $R_x$  or  $R_y$  to form a 3- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

Docket No.: 61387(72021)

such that R<sub>3</sub> is not an unsubstituted alkyl group;

- R<sub>4</sub> is independently selected at each occurrence from R<sub>b</sub>, or two adjacent R<sub>4</sub> groups are taken together to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>;
- $R_5$  is independently selected at each occurrence from hydrogen, hydroxy, halogen, amino, aminocarbonyl, cyano, nitro, -COOH,  $C_1$ - $C_6$ alkyl,  $\underline{C_2}$ - $\underline{C_6}$ alkenyl $\underline{C_4}$ - $\underline{C_6}$ alkenyl, cyano $\underline{C_1}$ - $\underline{C_6}$ alkynyl $\underline{C_4}$ - $\underline{C_6}$ alkynyl, halo $\underline{C_1}$ - $\underline{C_6}$ alkyl, amino $\underline{C_1}$ - $\underline{C_6}$ alkyl, cyano $\underline{C_1}$ - $\underline{C_6}$ alkyl,  $\underline{C_1}$ - $\underline{C_6}$ alkoxy, halo $\underline{C_1}$ - $\underline{C_6}$ alkoxy,  $\underline{C_1}$ - $\underline{C_8}$ alkanoyl,  $\underline{C_1}$ - $\underline{C_6}$ alkyl ether,  $\underline{C_1}$ - $\underline{C_6}$ alkoxycarbonyl, aminosulfonyl,  $\underline{C_1}$ - $\underline{C_6}$ alkyl)aminosulfonyl, mono- and di- $\underline{(C_1}$ - $\underline{C_6}$ alkyl)aminosulfonyl, mono- and di- $\underline{(C_1}$ - $\underline{C_6}$ alkyl)amino $\underline{C_0}$ - $\underline{C_4}$ alkyl; or two adjacent  $\underline{R_5}$  groups are taken together to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenylC<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynylC<sub>1</sub>-C<sub>8</sub>alkynyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino.
  - 17. (Original) A compound or salt according to claim 16, wherein Y is N.

18. (Currently amended) A compound or salt according to claim 16—or claim 17, wherein W is N and X is CR<sub>1</sub>.

Docket No.: 61387(72021)

- 19. (Currently amended) A compound or salt according to claim 16–or claim 17, wherein X is N and W is CR<sub>1</sub>.
- 20. (Currently amended) A compound or salt according to any one of claims 16-19claim 16, wherein n is 0.
- 21. (Currently amended) A compound or salt according to any one of claims 16-20 claim 16, wherein  $A_2$  and  $A_3$  are CH.
- 22. (Currently amended) A compound or salt according to <u>claim 16any</u> ene of claims 16-21, wherein  $A_1$  and  $A_4$  are independently N or CH.
- 23. (Currently amended) A compound or salt according to <u>claim 16-any</u> one of claims 16-22, wherein at least two of  $B_1$ ,  $B_2$ ,  $B_3$ ,  $B_4$  and  $B_5$  are  $CR_5$ , and wherein at least one  $R_5$  is not hydrogen.
- 24. (Currently amended) A compound or salt according to claim 23, wherein each  $R_5$  is independently chosen from hydrogen, halogen, cyano, -COOH,  $C_1$ - $C_6$ alkyl,  $C_2$ - $C_6$ alkenyl $C_1$ - $C_6$ alkenyl, halo $C_1$ - $C_6$ alkoxy and halo $C_1$ - $C_6$ alkoxy.
- 25. (Currently amended) A compound or salt according to <u>claim 16any</u> one of claims 16-24, wherein  $R_2$  is halogen, isopropyl, t-butyl, trifluoromethyl, methylsulfonyl, trifluoromethylsulfonyl or 2-cyano-prop-2-yl.
- 26. (Currently amended) A compound or salt according to <u>claim 16</u>any one of claims 16-25, wherein  $R_3$  is:
  - (a) hydrogen or cyano; or

Application No. 10/591,553 Docket No.: 61387(72021)

Amendment dated July 14, 2007

Page 10

First Preliminary Amendment

(b)  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl or (4- to 10-membered heterocycloalkyl) $C_0$ - $C_6$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ - $C_4$ alkyl, and halo $C_1$ - $C_4$ alkyl.

- 27. (Original) A compound or salt according to claim 26, wherein  $R_3$  is hydrogen.
- 28. (Original) A compound or salt according to claim 26, wherein  $R_3$  is  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl or (4- to 10-membered heterocycloalkyl) $C_0$ - $C_6$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, methyl and ethyl.
  - 29. (Currently amended) A compound of the formula:

or a pharmaceutically acceptable salt thereof, wherein:

n is 0 or 1;

W, X and Y are each independently N or CR<sub>1</sub>;

A<sub>1</sub> and A<sub>4</sub> are independently N or CH;

 $A_2$  and  $A_3$  are independently N or  $CR_4$ ; such that neither  $A_2$  nor  $A_3$  is  $C_1$ - $C_6$ alkyl if  $R_2$  is  $C_1$ - $C_6$ alkyl;

 $B_1$ ,  $B_2$ ,  $B_3$ ,  $B_4$  and  $B_5$  are each independently N or  $CR_5$ ; such that at least one of  $B_1$ ,  $B_2$ ,  $B_3$ ,  $B_4$  and  $B_5$  is a substituted carbon;

Docket No.: 61387(72021)

- $R_1$  is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, nitro, amino,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ alkoxycarbonyl, aminosulfonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl;
- $R_2 \text{ is halogen, cyano, amino, } C_3\text{-}C_6\text{alkyl, cyanoC}_1\text{-}C_6\text{alkyl, haloC}_1\text{-}C_6\text{alkyl, mono- or di-}\\ (C_1\text{-}C_6\text{alkyl)}\text{aminoC}_0\text{-}C_4\text{alkyl, } C_1\text{-}C_6\text{alkylsulfonyl, haloC}_1\text{-}C_6\text{alkylsulfonyl, mono- or di-}\\ (C_1\text{-}C_6\text{alkyl)}\text{aminosulfonyl, or mono- or di-}(C_1\text{-}C_6\text{alkyl})\text{aminocarbonyl;}$

R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:  $R_x$  is  $C_0$ - $C_3$ alkylene;
  - L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;
  - M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $\underline{C_8}$ alkenyl- $\underline{C_1}$ - $\underline{C_8}$ alkenyl-or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl $\underline{C_1}$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

# R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with  $R_x$  or  $R_z$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

Docket No.: 61387(72021)

- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 3- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;
- R<sub>4</sub> is independently selected at each occurrence from R<sub>b</sub>, or two adjacent R<sub>4</sub> groups are taken together to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>;
- $R_5$  is independently selected at each occurrence from hydrogen, hydroxy, halogen, amino, aminocarbonyl, cyano, nitro, -COOH,  $C_1$ - $C_6$ alkyl,  $C_2$ - $C_6$ alkenyl- $C_4$ - $C_6$ alkynyl,  $C_3$ - $C_8$ cycloalkyl, halo $C_1$ - $C_6$ alkyl, amino $C_1$ - $C_6$ alkyl, cyano $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_8$ alkanoyl,  $C_1$ - $C_8$ alkanoyloxy,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether,  $C_1$ - $C_6$ alkoxycarbonyl, aminosulfonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminocarbonyl, and mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl; or two adjacent  $R_5$  groups are taken together to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and
- (ii)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl $C_1$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl $C_1$ - $C_8$ alkynyl,  $C_3$ - $C_8$ cycloalkyl, halo $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkoxy, halo $C_1$ - $C_8$ alkoxy,  $C_1$ - $C_8$ alkanoyl,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether,  $C_1$ - $C_6$ alkoxycarbonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono-

and di-( $C_1$ - $C_6$ alkyl)aminosulfonyl, mono- and di-( $C_1$ - $C_6$ alkyl)aminocarbonyl, and mono- and di-( $C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano,  $C_1$ - $C_4$ alkyl,  $C_1$ - $C_4$ alkoxy, hydroxy $C_1$ - $C_4$ alkyl, halo $C_1$ - $C_4$ alkyl, and mono- and di-( $C_1$ - $C_4$ alkyl)amino.

Docket No.: 61387(72021)

- 30. (Original) A compound or salt according to claim 29, wherein Y is N.
- 31. (Currently amended) A compound or salt according to claim 29—or claim 30, wherein W is N and X is CR<sub>1</sub>.
- 32. (Currently amended) A compound or salt according to claim 29-or claim 30, wherein X is N and W is CR<sub>1</sub>.
- 33. (Currently amended) A compound or salt according to <u>claim 29</u><del>any</del> one of claims 29-32, wherein n is 0.
  - 34. (Cancelled)
- 35. (Currently amended) A compound or salt according to <u>claim 29</u> any one of claims 29-34, wherein one or both of  $B_1$  and  $B_5$  is  $CR_5$ , and wherein  $R_5$  at  $B_1$  or  $B_5$  is not hydrogen.
- 36. (Currently amended) A compound or salt according to <u>claim 29any</u> one of claims 29-35, wherein each  $R_5$  is independently chosen from hydrogen, halogen, cyano, -COOH,  $C_1$ - $C_6$ alkyl,  $\underline{C_2$ - $\underline{C_6}$ alkenyl $\underline{C_1$ - $\underline{C_6}$ alkenyl, halo $\underline{C_1$ - $\underline{C_6}$ alkoxy and halo $\underline{C_1$ - $\underline{C_6}$ alkoxy.
- 37. (Currently amended) A compound or salt according to <u>claim 29any</u> one of claims 29-36, wherein  $R_2$  is halogen, isopropyl, t-butyl, trifluoromethyl, methylsulfonyl, trifluoromethylsulfonyl or 2-cyano-prop-2-yl.

38. (Currently amended) A compound or salt according to  $\frac{29}{\text{any}}$  one of claims 29-37, wherein  $R_3$  is:

Docket No.: 61387(72021)

- (a) hydrogen, halogen or cyano; or
- (b)  $C_1$ - $C_6$ alkyl,  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl or (4- to 10-membered heterocycloalkyl) $C_0$ - $C_6$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ - $C_4$ alkyl, and halo $C_1$ - $C_4$ alkyl.
- 39. (Original) A compound or salt according to claim 38, wherein  $R_3$  is hydrogen.
- 40. (Original) A compound or salt according to claim 38, wherein  $R_3$  is  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl or (4- to 10-membered heterocycloalkyl) $C_0$ - $C_6$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, methyl and ethyl.
  - 41. (Currently amended) A compound of the formula:

$$\begin{array}{c} A_2 \\ A_3 \\ A_3 \\ A_4 \\ A_5 \\ A_5 \\ A_6 \\ A_7 \\ A_8 \\$$

or a pharmaceutically acceptable salt thereof, wherein:

W and X are independently N or  $CR_1$ , such that at least one of W and X is N;

A<sub>2</sub> and A<sub>3</sub> are each CR<sub>4</sub>;

 $B_1$ ,  $B_2$  and  $B_3$  are  $CR_5$ ; such that at least one  $R_5$  is not hydrogen;

B<sub>5</sub> is N or CH;

 $R_1$ , if present, is hydrogen or methyl;

 $R_2$  is halogen, isopropyl, t-butyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkylsulfonyl, hydroxy $C_1$ - $C_6$ alkyl or cyano $C_1$ - $C_6$ alkyl;  $R_3$  is:

Docket No.: 61387(72021)

- (a) hydrogen, halogen or cyano; or
  - (b)  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl or (4- to 10-membered heterocycloalkyl) $C_0$ - $C_6$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ - $C_4$ alkyl, and halo $C_1$ - $C_4$ alkyl;

each  $R_4$  is independently chosen from methyl, halogen and hydrogen; and each  $R_5$  is independently chosen from hydrogen, halogen, cyano, -COOH,  $C_1$ - $C_6$ alkyl,  $C_2$ - $C_6$ alkenyl $C_4$ - $C_6$ alkenyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy and halo $C_1$ - $C_6$ alkoxy.

- 42. (Currently amended) A compound or salt according to <u>claim 1 any</u> one of claims 1-41, wherein the compound has an  $IC_{50}$  value of 1 micromolar or less in a capsaicin receptor calcium mobilization assay.
- 43. (Currently amended) A compound or salt according to <u>claim 1</u> any one of claims 1-41, wherein the compound has an IC<sub>50</sub> value of 100 nanomolar or less in a capsaicin receptor calcium mobilization assay.

### 44. (Cancelled)

- 45. (Currently amended) A pharmaceutical composition, comprising at least one compound or salt according to <u>claim 1 any one of claims 1-41</u>, in combination with a physiologically acceptable carrier or excipient.
- 46. (Original) A pharmaceutical composition according to claim 45, wherein the composition is formulated as an injectible fluid, an aerosol, a cream, a gel, a pill, a capsule, a syrup or a transdermal patch.

Page 16

47. (Currently amended) A method for reducing calcium conductance of a cellular capsaicin receptor, comprising contacting a cell expressing a capsaicin receptor with at least one compound of the formula:

Docket No.: 61387(72021)

or a pharmaceutically acceptable salt thereof, wherein:

 $Ar_1$  is a phenyl, benzyl or a 5- or 6-membered heteroaryl or (heteroaryl)methyl group, each of which is substituted with from 0 to 5 substituents independently chosen from  $R_b$  and groups that are taken together to form a fused 5- or 6-membered carbocycle or heterocycle that is substituted with from 0 to 5 substituents independently chosen from  $R_b$ ;

Ar<sub>2</sub> is phenyl, naphthyl or a 5- to 10-membered heteroaryl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub>;

W, X and Y are each independently N or CR<sub>1</sub>;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, cyano, nitro, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, aminocarbonyl, aminosulfonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl;

R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>),  $N(R_z)(C=O)_p$ , SO<sub>2</sub>N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $\underline{C_8}$ alkenyl- $\underline{C_1}$ - $\underline{C_8}$ alkenyl-or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl $\underline{C_1}$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

Docket No.: 61387(72021)

## R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

#### R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with  $R_x$  or  $R_y$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

R<sub>b</sub> is independently chosen at each occurrence from:

(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenylC<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynylC<sub>1</sub>-C<sub>8</sub>alkynyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

Docket No.: 61387(72021)

and thereby reducing calcium conductance of the capsaicin receptor.

- 48. (Currently amended) A method according to claim 47, wherein the compound is a compound according to claim 1 any one of claims 1-41.
- 49. (Original) A method according to claim 47, wherein the cell is contacted *in vivo* in an animal.
- 50. (Original) A method according to claim 49, wherein the cell is a neuronal cell.
- 51. (Original) A method according to claim 49, wherein the cell is a urothelial cell.
- 52. (Original) A method according to claim 49, wherein during contact the compound is present within a body fluid of the animal.
- 53. (Original) A method according to claim 49, wherein the compound is present in the blood of the animal at a concentration of 1 micromolar or less.
  - 54. 55. (Cancelled)
- 56. (Original) A method according to claim 49, wherein the animal is a human.
- 57. (Original) A method according to claim 49, wherein the compound is administered orally.
  - 58. 62. (Cancelled)

Page 19

63. (Original) A method according to claim 60, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

64. (Currently amended) A method for treating a condition responsive to capsaicin receptor modulation in a patient, comprising administering to the patient a therapeutically effective amount of at least one compound of the formula:

$$X \xrightarrow{\text{HN}} R_3$$

or a pharmaceutically acceptable salt thereof, wherein:

 $Ar_1$  is a phenyl, benzyl or a 5- or 6-membered heteroaryl or (heteroaryl)methyl group, each of which is substituted with from 0 to 5 substituents independently chosen from  $R_b$  and groups that are taken together to form a fused 5- or 6-membered carbocycle or heterocycle that is substituted with from 0 to 5 substituents independently chosen from  $R_b$ ;

Ar<sub>2</sub> is phenyl, naphthyl or a 5- to 10-membered heteroaryl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub>;

W, X and Y are each independently N or CR<sub>1</sub>;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, cyano, nitro, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, aminocarbonyl, aminosulfonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl;

R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:  $R_x$  is  $C_0$ - $C_3$ alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S,  $SO_2$ , (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>,  $SO_2N(R_z)$ , or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $\underline{C_8}$ alkenyl  $\underline{C_1$ - $\underline{C_8}$ alkenyl or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl  $\underline{C_1$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

Docket No.: 61387(72021)

## R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

#### R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with  $R_x$  or  $R_y$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

R<sub>b</sub> is independently chosen at each occurrence from:

(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and

Application No. 10/591,553 Docket No.: 61387(72021)

Amendment dated July 14, 2007

Page 21

First Preliminary Amendment

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, <u>C<sub>2</sub>-C<sub>8</sub>alkenylC<sub>1</sub>-C<sub>8</sub>alkenyl</u>, <u>C<sub>2</sub>-C<sub>8</sub>alkynylC<sub>1</sub>-C<sub>8</sub>alkynyl</u>, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

and thereby alleviating the condition in the patient.

- 65. (Currently amended) A method according to claim 64, wherein the compound is a compound according to claim 1 any one of claims 1-41.
- 66. (Original) A method according to claim 64, wherein the patient is suffering from (i) exposure to capsaicin, (ii) burn or irritation due to exposure to heat, (iii) burns or irritation due to exposure to light, (iv) burn, bronchoconstriction or irritation due to exposure to tear gas, infectious agents, air pollutants or pepper spray, or (v) burn or irritation due to exposure to acid.
- 67. (Original) A method according to claim 64, wherein the condition is asthma or chronic obstructive pulmonary disease.
- 68. (Currently amended) A method for treating pain in a patient, comprising administering to a patient suffering from pain a therapeutically effective amount of at least one compound of the formula:

or a pharmaceutically acceptable salt thereof, wherein:

Ar<sub>1</sub> is a phenyl, benzyl or a 5- or 6-membered heteroaryl or (heteroaryl)methyl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub> and groups that are taken together to form a fused 5- or 6-membered

carbocycle or heterocycle that is substituted with from 0 to 5 substituents independently chosen from  $R_b$ ;

Docket No.: 61387(72021)

Ar<sub>2</sub> is phenyl, naphthyl or a 5- to 10-membered heteroaryl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub>;

W, X and Y are each independently N or CR<sub>1</sub>;

 $R_1$  is independently selected at each occurrence from hydrogen, halogen, cyano, nitro, amino,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ alkoxycarbonyl, aminocarbonyl, aminosulfonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl;

R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:  $R_x$  is  $C_0$ - $C_3$ alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, <u>C<sub>2</sub>-C<sub>8</sub>alkenyl C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>2</sub>-C<sub>8</sub>alkynyl C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and</u>

R<sub>v</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with  $R_x$  or  $R_z$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

Docket No.: 61387(72021)

### R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, <u>C<sub>2</sub>-C<sub>8</sub>alkenylC<sub>1</sub>-C<sub>8</sub>alkenyl</u>, <u>C<sub>2</sub>-C<sub>8</sub>alkynylC<sub>1</sub>-C<sub>8</sub>alkynyl</u>, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

and thereby alleviating pain in the patient.

69. (Currently amended) A method according to claim 68, wherein the compound is a compound according to claim 1<del>any one of claims 1-41</del>.

Page 24

70. (Original) A method according to claim 68, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

Docket No.: 61387(72021)

71. – 72. (Cancelled)

- 73. (Original) A method according to claim 68, wherein the patient is suffering from neuropathic pain.
- 74. (Original) A method according to claim 68, wherein the pain is associated with a condition selected from: postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, toothache, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, neuritis, neuronitis, neuralgia, AIDS-related neuropathy, MS-related neuropathy, spinal cord injury-related pain, surgery-related pain, musculoskeletal pain, back pain, headache, migraine, angina, labor, hemorrhoids, dyspepsia, Charcot's pains, intestinal gas, menstruation, cancer, venom exposure, irritable bowel syndrome, inflammatory bowel disease and trauma.
- 75. (Original) A method according to claim 68, wherein the patient is a human.
- 76. (Currently amended) A method for treating itch in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:

$$X \xrightarrow{HN} \xrightarrow{Ar_2} N \\ X \xrightarrow{N} \xrightarrow{N} Y \xrightarrow{R_3} R_3$$

or a pharmaceutically acceptable salt thereof, wherein:

Ar<sub>1</sub> is a phenyl, benzyl or a 5- or 6-membered heteroaryl or (heteroaryl)methyl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub> and groups that are taken together to form a fused 5- or 6-membered

carbocycle or heterocycle that is substituted with from 0 to 5 substituents independently chosen from  $R_b$ ;

Docket No.: 61387(72021)

Ar<sub>2</sub> is phenyl, naphthyl or a 5- to 10-membered heteroaryl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub>;

W, X and Y are each independently N or CR<sub>1</sub>;

 $R_1$  is independently selected at each occurrence from hydrogen, halogen, cyano, nitro, amino,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ alkoxycarbonyl, aminocarbonyl, aminosulfonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl;

R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:  $R_x$  is  $C_0$ - $C_3$ alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $\underline{C_8}$ alkenyl  $\underline{C_1$ - $\underline{C_8}$ alkenyl or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl $\underline{C_1$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

> (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

Docket No.: 61387(72021)

### R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, <u>C<sub>2</sub>-C<sub>8</sub>alkenylC<sub>1</sub>-C<sub>8</sub>alkenyl</u>, <u>C<sub>2</sub>-C<sub>8</sub>alkynylC<sub>1</sub>-C<sub>8</sub>alkynyl</u>, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

and thereby alleviating itch in the patient.

77. (Currently amended) A method according to claim 76, wherein the compound is a compound according to <u>claim 1 any one of claims 1-41</u>.

Page 27

78. (Currently amended) A method for treating cough or hiccup in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:

Docket No.: 61387(72021)

or a pharmaceutically acceptable salt thereof, wherein:

 $Ar_1$  is a phenyl, benzyl or a 5- or 6-membered heteroaryl or (heteroaryl)methyl group, each of which is substituted with from 0 to 5 substituents independently chosen from  $R_b$  and groups that are taken together to form a fused 5- or 6-membered carbocycle or heterocycle that is substituted with from 0 to 5 substituents independently chosen from  $R_b$ ;

Ar<sub>2</sub> is phenyl, naphthyl or a 5- to 10-membered heteroaryl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub>;

W, X and Y are each independently N or CR<sub>1</sub>;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, cyano, nitro, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, aminocarbonyl, aminosulfonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl;

R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:  $R_x$  is  $C_0$ - $C_3$ alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S,  $SO_2$ , (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>,  $SO_2$ N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $\underline{C_8}$ alkenyl  $\underline{C_1$ - $\underline{C_8}$ alkenyl or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl  $\underline{C_1$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

Docket No.: 61387(72021)

## R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

#### R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with  $R_x$  or  $R_y$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

R<sub>b</sub> is independently chosen at each occurrence from:

(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and

Page 29

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, <u>C<sub>2</sub>-C<sub>8</sub>alkenylC<sub>1</sub>-C<sub>8</sub>alkenyl</u>, <u>C<sub>2</sub>-C<sub>8</sub>alkynylC<sub>1</sub>-C<sub>8</sub>alkynyl</u>, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

Docket No.: 61387(72021)

and thereby alleviating cough or hiccup in the patient.

- 79. (Currently amended) A method according to claim 78, wherein the compound is a compound according to claim 1 any one of claims 1-41.
- 80. (Currently amended) A method for treating urinary incontinence or overactive bladder in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:

or a pharmaceutically acceptable salt thereof, wherein:

 $Ar_1$  is a phenyl, benzyl or a 5- or 6-membered heteroaryl or (heteroaryl)methyl group, each of which is substituted with from 0 to 5 substituents independently chosen from  $R_b$  and groups that are taken together to form a fused 5- or 6-membered carbocycle or heterocycle that is substituted with from 0 to 5 substituents independently chosen from  $R_b$ ;

Ar<sub>2</sub> is phenyl, naphthyl or a 5- to 10-membered heteroaryl group, each of which is substituted with from 0 to 5 substituents independently chosen from R<sub>b</sub>;

W, X and Y are each independently N or CR<sub>1</sub>;

 $R_1$  is independently selected at each occurrence from hydrogen, halogen, cyano, nitro, amino,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy,  $C_1$ - $C_6$ alkoxycarbonyl, aminocarbonyl, aminosulfonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl;

Docket No.: 61387(72021)

### R<sub>3</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula  $-R_x$ -L-M- $R_y$ , wherein:  $R_x$  is  $C_0$ - $C_3$ alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>),  $N(R_z)(C=O)_p$ , SO<sub>2</sub>N(R<sub>z</sub>), or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $\underline{C_2$ - $\underline{C_8}$ alkenyl- $\underline{C_1}$ - $\underline{C_8}$ alkenyl-or  $\underline{C_2}$ - $\underline{C_8}$ alkynyl $\underline{C_1}$ - $\underline{C_8}$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

## R<sub>v</sub> is:

- (a) hydrogen;
- (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkoxy,  $(C_1$ - $C_8$ alkyl)amino $C_0$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkanoyl,  $C_3$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or
- (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

#### Rz is:

(a) hydrogen;

(b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkanoyl,  $C_3$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 3- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or

Docket No.: 61387(72021)

(c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and –COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, <u>C<sub>2</sub>-C<sub>8</sub>alkenyl</u>C<sub>1</sub>-C<sub>8</sub>alkenyl, <u>C<sub>2</sub>-C<sub>8</sub>alkynyl</u>C<sub>1</sub>-C<sub>8</sub>alkynyl, C<sub>3</sub>-C<sub>8</sub>cycloalkyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>6</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, monoand di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminocarbonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

and thereby alleviating urinary incontinence or overactive bladder in the patient.

- 81. (Currently amended) A method according to claim 80, wherein the compound is a compound according to claim 1 any one of claims 1-41.
  - 82. 86. (Cancelled)
  - 87. (Original) A packaged pharmaceutical preparation, comprising:
  - (a) a pharmaceutical composition according to claim 45 in a container; and

- (b) instructions for using the composition to treat pain.
- 88. (Original) A packaged pharmaceutical preparation, comprising:
- (a) a pharmaceutical composition according to claim 45 in a container; and
  - (b) instructions for using the composition to treat cough or hiccup.

Docket No.: 61387(72021)

- 89. (Cancelled)
- 90. (Original) A packaged pharmaceutical preparation, comprising:
- (a) a pharmaceutical composition according to claim 45 in a container; and
- (b) instructions for using the composition to treat urinary incontinence or overactive bladder.
  - 91. 92. (Cancelled)